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EDITORIAL COMMENT

# Is It Time to Jettison Complex Mechanical Thrombectomy in Favor of Simple Manual Aspiration Devices?*

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Thrombus extraction at the time of percutaneous intervention in patients with acute myocardial infarction is an intuitively attractive therapy. From a pathophysiological standpoint, reduction of thrombus burden before coronary stent implantation can reduce distal microcirculatory embolization, lower the incidence of subsequent no-reflow phenomena, and improve myocardial reperfusion and salvage (1). Recent data from randomized clinical trials supporting the use of thrombus extraction in primary percutaneous intervention (2–4) have led to increased uptake of this technology in routine clinical practice and prompted the endorsement of thrombus extraction devices (Level of Evidence: B) in a focused update of guidelines on management of patients with ST-segment elevation myocardial infarction (5).

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The apparent benefit associated with thrombus extraction in primary intervention requires qualification by the observation that benefit is unlikely to be a class effect. In particular, clinicians have 2 principal categories of thrombus extraction approaches at their disposal: 1) mechanical thrombectomy devices (e.g., AngioJet, Rescue, Xsizer); and 2) manual or aspiration thrombectomy devices (e.g., Diver, Export, Pronto). Indeed, in the case of 2 recent large-scale meta-analyses demonstrating a mortality benefit for patients randomized to thrombus extraction as opposed to those managed with conventional primary intervention, this effect appeared to be confined to patients treated with manual thrombectomy devices (6,7). This evidence of differential efficacy is reflected in the guidelines, which restrict their endorsement of thrombus extraction to manual aspiration devices only (5).

The AngioJet thrombectomy system (Medrad Interventional/Possis, Minneapolis, Minnesota) consists of a hollow catheter with a high-pressure hypotube through which saline is pumped to the catheter tip, exiting in a series of high-speed jets that are directed retrograde over a mouth just proximal to the catheter tip. The action of the jets creates a localized vacuum on the basis of the Bernouilli/Venturi effect, drawing thrombus into the hollow catheter interior, where it is mechanically disrupted and evacuated from the body. The device was approved by the Food and Drug Administration in June 1998 on the basis of encouraging results among patients with acute coronary syndromes enrolled in the VeGAS (Vein Graft AngioJet Studies)-1 and -2 trials (8). However, in the subsequent AIMI (AngioJet Rheolytic Thrombectomy in Patients Undergoing Primary Angioplasty for Acute Myocardial Infarction) trial, randomization to thrombectomy in comparison with conventional primary intervention was associated with an increase in infarct size, a reduction in Thrombolysis In Myocardial Infarction (TIMI) flow grade 3 and a higher incidence of 30-day adverse clinical outcomes (9).

In this issue of the *Journal*, Migliorini et al. (10) present the results of a randomized comparison between mechanical thrombectomy with the AngioJet rheolytic thrombectomy catheter and conventional therapy in 501 patients undergoing primary direct stenting for myocardial infarction with ST-segment elevation. The JETSTENT (AngioJet Rheolytic Thrombectomy Before Direct Infarct Artery Stenting in Patients Undergoing Primary PCI for Acute Myocardial Infarction) investigators have considerable experience in the field of thrombus extraction therapy and are highly qualified for exploring the role of this therapy in the setting of a multicenter randomized controlled trial. The main finding of this trial is that the authors were unable to discard their null hypothesis (i.e., that there was no difference between the 2 treatment strategies) with respect to the coprimary end points of ST-segment elevation resolution and scintigraphic infarct size. More specifically, a trend toward more frequent ST-segment resolution with rheolytic thrombectomy (85.8% vs. 78.8%, $p = 0.043$) was not significant in view of the penalty incurred for multiple primary comparisons. In addition, there was no signal of a difference between the 2 strategies with regard to scintigraphically determined infarct size (11.8% vs. 12.75%, $p = 0.40$). Regarding the additional surrogate end points, if anything, a trend was seen in the other direction, with numerically lower incidence of both coronary flow grade 3 and myocardial blush grade 3 as assessed by TIMI criteria in the rheolytic thrombectomy group.

In terms of clinical outcomes, significant differences were observed in favor of the mechanical thrombectomy arm regarding the composite of major adverse events at 6 and 12

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**Table 1** Major Features and Findings of 2 Largest Trials on Value of Angiojet Thrombectomy System

| | JETSTENT Trial (n = 501) | | AIMI Trial (n = 480) | |
|---|---|---|---|---|
| | Rheolytic Thrombectomy | Control | Rheolytic Thrombectomy | Control |
| Angiographic evidence of thrombus as an inclusion criterion | Yes | Yes | No | No |
| ST-segment elevation resolution* | 85.8% | 78.8% | 60% | 68% |
| Post-procedural TIMI flow grade 3 | 80.6% | 85.9% | 91.8% | 97.0% |
| Post-procedural TIMI blush grade 3 | 72.1% | 79.1% | 30.6% | 36.8% |
| Scintigraphic infarct size† | 11.8% | 12.75% | 12.5% | 9.8% |
| 30-day incidence of MACE | 3.1% | 6.9% | 6.7% | 1.7% |

*The ST-segment elevation resolution was defined as a reduction in ST-segment elevation of ≥50% in the JETSTENT trial and >70% in the AIMI trial. †Infarct size was shown as a median value in the JETSTENT trial and as mean value in the AIMI trial.

AIMI = Angiojet Rheolytic Thrombectomy in Patients Undergoing Primary Angioplasty for Acute Myocardial Infarction; JETSTENT = AngioJet Rheolytic Thrombectomy Before Direct Infarct Artery Stenting in Patients Undergoing Primary PCI for Acute Myocardial Infarction; MACE = major adverse cardiovascular events; TIMI = Thrombolysis In Myocardial Infarction.

months. On 1 level, these results are difficult to reconcile with the lack of clear benefit in surrogate markers of microcirculatory function. Furthermore, the interpretation of secondary end points in trials with a negative primary end point always entails considerable hazard. Against this, it might be observed that these differences are due in large part to differences in clinical restenosis—a microcirculatory-independent benefit of thrombectomy consequent on more accurate lesion assessment, as evidenced by significantly lower number of stents and total stented length in the thrombectomy arm. Notably, the JETSTENT study was an exclusively bare-metal stent study, and the increasing evidence in support of drug-eluting stents in acute myocardial infarction might be expected to dilute the benefit of this effect (11).

The major features and findings of the 2 largest trials on the value of the AngioJet thrombectomy system—the present JETSTENT trial (10) and the older AIMI trial (9)—are summarized in Table 1. A key difference between the trials is that the investigators of the JETSTENT trial enrolled only patients with angiographic evidence of thrombus, which certainly increases the chances of success of thrombectomy devices. In terms of results, these 2 trials are in line in showing no reduction in infarct size and more unfavorable indicators of epicardial and myocardial flow with rheolytic thrombectomy. However, whereas both ST-segment resolution and clinical end points in the AIMI trial were consistent and followed the direction seen in the flow parameters, the JETSTENT trial showed enhanced ST-segment resolution and improved clinical outcomes with rheolytic thrombectomy. One possible explanation is that although the prognostic value of surrogate end points has been validated by large studies, their accuracy is also sensitive to the assessment method. Furthermore, both of these trials were largely underpowered for the analysis of clinical end points, leading to broad and overlapping confidence intervals. The investigators of the JETSTENT trial are absolutely right to advocate the need for larger clinical trials using the AngioJet device, but considering the slow enrollment rate in their multicenter trial, the chances of such a trial coming to pass seem very low.

In light of the often superior thrombus extraction efficiency with mechanical thrombectomy, what explains the disappointing outcomes with mechanical devices in general and the JETSTENT trial in particular? At least 2 possible explanations should be considered. First, mechanical thrombectomy devices are considerably more complex to operate than manual aspiration catheters. They tend to be bulkier, have longer learning curves, require considerably lengthened procedure times, and their use is more often restricted by coronary anatomy. The relevance of these issues is amplified in the setting of acute myocardial infarction, which is often performed out-of-hours, with reduced staffing capabilities and higher rates of procedural complications. Second, the rheolytic thrombectomy catheter has some specific limitations, which include: 1) a propensity to impair rather than enhance distal microcirculatory perfusion (as discussed in the preceding text); and 2) a recommendation for prophylactic temporary pacemaker implantation due to a high incidence of symptomatic bradycardia (likely due to hemolysis-induced distal adenosine release, especially relevant when the infarct-related artery is a dominant right coronary or circumflex artery). A notable feature of the current study is that the investigators addressed these latter device-specific concerns by dispensing with the traditional approach of first crossing the culprit lesion and then engaging the device with a retrograde pullback. Their employment of a single anterograde pass technique may underlie the very low rate of temporary pacemaker deployment in the current study.

The results with manual thrombectomy devices are far more encouraging than those with mechanical thrombus extraction (2–4,6,7). In general, the devices are considerably more user-friendly, and consequently have shorter learning curves. Nevertheless, a number of issues relating to the more precise role of thrombus extraction in primary intervention for myocardial infarction remain open. For example, should a strategy of universal device usage in the culprit lesion of all patients with ST-segment elevation—as undertaken in TAPAS (Thrombus Aspiration During Percutaneous Coronary Intervention in Acute Myocardial Infarction Study) (4)—be preferred to an intuitively more reasonable selective

patient approach? And if a selective strategy is employed, which patients are likely to benefit most? Patients with visible and large thrombus burden of the culprit vessel are obviously the optimal candidates, especially if they present with shorter ischemic times.

## Conclusions

The JETSTENT investigators are to be commended for a well-designed and executed study in an effort to further help patients with acute myocardial infarction undergoing percutaneous coronary intervention. However, the authors' enthusiastic interpretation of the results may be driven more by their attraction to the concept of thrombectomy than by the strength of the evidence shown in the study. Device complexity may be a significant limitation of rheolytic thrombectomy, especially in out-of-hours and emergency situations, and what evidence is available is far from being a motivation for its adoption into routine practice. In keeping with the findings of recent meta-analyses and in line with current guideline recommendations, the message emerging is clear: thrombus extraction seems to be a useful adjunctive therapy for patients undergoing primary percutaneous coronary intervention for ST-segment elevation myocardial infarction, and the modality of choice appears to be simple manual aspiration.

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